Factors of Importance in the Use of Triethylene Glycol Vapor for Aerial Disinfection*

WILLIAM LESTER, Jr., M.D., SAUL KAYE, O. H. ROBERTSON, M.D., and EDWARD W. DUNKLIN

Assistant Professor; Research Associate; Professor of Medicine; and Research Assistant; Department of Medicine, University of Chicago, Chicago, Ill.

At the present time acute respiratory diseases account for a very significant proportion of potentially preventable human illness and their effects represent a substantial economic loss to society. The probable relationship of many of these diseases to the air-borne route of contagion has stimulated the development of techniques of aerial disinfection. Since popular interest in such methods has been aroused by reports of the germicidal action of the vapors of various chemical compounds, it is thought timely to summarize briefly the present knowledge concerning one of these agents, namely, triethylene glycol.

The first report of the bactericidal effect of triethylene glycol vapor on air-borne microörganisms was made by Robertson and his associates in 1943.[1] Earlier studies[2–7] had been made utilizing propylene glycol vapor in which rapid killing of air-borne pathogens was demonstrated. However, when an evaluation of related compounds was made, triethylene glycol was found to be most suitable because smaller concentrations were required.

Triethylene glycol is a glycol-ether of the following structure: $HOCH_2CH_2OCH_2CH_2OCH_2CH_2OH$. It has a boiling point of 290° C. and a vapor pressure of 0.001 mm. Hg at 22° C. Pure triethylene glycol is odorless and tasteless and is an extremely hygroscopic substance. Because of its low vapor pressure, vaporization is usually accomplished by heating. Triethylene glycol vapor has no deleterious effect on fabrics, books or surfaces in the environment in which it is present.

In vitro studies[8] have shown that triethylene glycol has a moderate germicidal potency against broth cultures of respiratory pathogens. The bactericidal action does not become apparent until concentrations greater than 20 per cent by volume are used. Thus, the *in vitro* germicidal action of triethylene glycol is of a much lower order of magnitude than that of the commonly used disinfecting agents. An interesting phenomenon was noted, namely, that a minimum quantity of water is necessary for rapid lethal action. This finding may be of significance in terms of the mechanism of action of the glycols.

Under controlled laboratory conditions, triethylene glycol vapor has been found to exert a rapid lethal action against a wide variety of air-borne infectious agents. The bacteria found to be susceptible to glycol vapor include pneumococci, Types I, II, and III; beta-

* Presented at a Joint Session of the American School Health Association and the Engineering, Epidemiology, Industrial Hygiene, and School Health Sections of the American Public Health Association at the Seventy-seventh Annual Meeting in New York, N. Y., October 28, 1949.

hemolytic streptococci, Groups A and C; alpha streptococci; staphylococci; influenza bacilli; *Escherichia coli;* and *Bacillus aerogenes.*[1, 9] The virucidal effects of triethylene glycol vapor have been demonstrated against the viruses of influenza, PR8 strain[1]; meningopneumonitis[10]; and psittacosis.[11] Bigg and Mellody[12] have reported on the fungicidal action of high concentrations of triethylene glycol vapor. Further studies will result in useful information concerning the susceptibility of other air-borne infectious agents.

Experiments designed to evaluate the toxicity of triethylene glycol by inhalation and ingestion in monkeys and rats have been reported.[13] These tests were carried on for more than a year and no evidence of significant toxicity was obtained. Because the amounts necessary for bactericidal action in the air are so minute, the quantity of triethylene glycol retained by inhalation never approaches a toxic level.

The mechanism of aerial disinfection by the glycols was analyzed in detail by Puck,[14] and he demonstrated that it is the vapor phase which is essential for such action to occur. Puck stated that "the effectiveness of any compound as an aerial germicide depends upon the extent of condensation of its vapor on air-suspended bacteria, and on the rate at which the resulting concentration of germicide can produce death of the microörganisms." A low vapor pressure, high hygroscopicity, and toxicity for bacterial metabolism were the properties cited by Puck as being required of a compound if it were to be an efficient aerial disinfectant. It can be seen that triethylene glycol adequately fulfils two of these criteria and, although a weak germicide, is sufficiently toxic to produce effective killing.

Wise, Puck, and Stral[15] have developed a method for determining the triethylene glycol content of the air. The air is bubbled through water, and the aqueous solution of glycol thus obtained is mixed with a solution of potassium dichromate in sulfuric acid. The extent of reduction of the dichromate solution is proportional to the concentration of glycol in the air. While useful, this method is not specific, and requires the sampling of large quantities (ca 300 liters) of air. Recently, a more sensitive test has been developed[16] in which concentrated sulfuric acid is used as the sampling medium. The acid, containing triethylene glycol, is treated with alpha-naphthol; and the depth of the yellow color formed is proportional to the concentration of the glycol. Usually, only 30 liters of air are required for a sample. It is reported that this test has an accuracy of 5 per cent in the range of 1 to 10 micrograms of glycol per liter of air. The characteristics of air containing both glycol and water vapor form the basis of an analytical instrument called a "glycostat" or "glycometer."[17] This instrument is primarily a research tool at present. It is quite complex and expensive and, while it has been in use in our laboratories for a number of years, it is not yet commercially available.

Factors which determine the availability of triethylene glycol vapor for condensation upon air-borne particles will influence the rate at which aerial disinfection can occur. The concentration of glycol vapor in the environment, relative humidity, temperature, and rate of ventilation all affect the attainment of a satisfactory disinfection rate. Because of the importance of these features, each will be discussed in some detail.

CONCENTRATION OF GLYCOL VAPOR

Minute quantities of triethylene glycol vapor (2 to 5 μg. per liter of air) are sufficient to produce maximal rates of bactericidal action. The explanation for this lies in the low vapor pressure of the glycol which leads to saturation of the air with low concentrations. The more closely the saturation level is approached, the greater will be the extent of condensation of glycol vapor on particles suspended in the air and, consequently, the more rapid the destruction of air-borne microörganisms. Fogging will become apparent if the concentration of glycol is kept near or above the saturation level. Thus, the appearance of a pronounced fog may be taken as evidence of excessive vaporization of glycol. However, in environments where no means of control of the glycol concentration are available, the presence of a slight fog will be the only indication that adequate amounts of vapor are present in the air. Aside from esthetic reasons, there is no harm inherent in such a fog.

RELATIVE HUMIDITY

The concentration of triethylene glycol vapor which saturates the air is determined by the relative humidity. Thus, at 0 per cent relative humidity the air is capable of containing a maximal amount of glycol vapor determined by the vapor pressure of pure triethylene glycol—8.5 μg. per liter at 22° C.[18] However, at 100 per cent humidity no glycol can be present in the vapor state. Furthermore, the relative humidity limits the maximum concentration of glycol which can accumulate within the airborne particle. The glycol-water content of the particle must always maintain an equilibrium with the vapor concentrations of these substances in the air. This latter phenomenon has practical significance because there are data available[19] to indicate that glycol vapor is much less effective at humidities above 60 per cent.

In summary, it may be stated that the relative humidity plays a dual role in determining the bactericidal action of glycol vapor, in that (1) it controls the saturation concentration according to physico-chemical principles; and (2) at high humidities the particles in equilibrium contain so much water that highly bactericidal concentrations of glycol are unattainable.

The data obtained from experiments utilizing atomized broth cultures of Group C hemolytic streptococci under controlled conditions indicate that maximum rates of bactericidal action of triethylene glycol vapor will be secured at humidities ranging from 20 to 50 per cent and at concentrations above 50 per cent saturation (2–5 μg. per liter).[19] When the particles containing the microorganisms have been subjected to prolonged desiccation, experimental data suggest that somewhat higher humidities are compatible with effective rates of kill, provided adequate concentrations of vapor are maintained.[20]

EFFECT OF TEMPERATURE

The influence of environmental temperature has been studied within the range of 55 to 85° F.[19] These levels were selected because they represent the extremes encountered in human habitations. There was a progressive increase in the rate of bactericidal action as the temperature was increased. At a constant saturation level of glycol vapor there was found to be approximately a twofold increase in the rate of bactericidal action with each 15° F. of thermal rise.

EFFECT OF VENTILATION

Another factor of importance in the attainment of adequate rates of aerial disinfection with glycol vapor is the quantity and quality of ventilation in the treated environment. Obviously, the rate of ventilation as determined by air changes per hour must be considered in the calculation of vapor outputs to be used. Under conditions of constant output of vapor, the loss of vapor due to air exchange is exponential and can represent an obstacle to the maintenance of adequate bactericidal concentrations. For example, assuming a ventilation rate of 1.5 air changes per hour and a constant rate of production of vapor, at the end of one hour 77 per cent of the vapor produced has been lost by ventilation alone. At 3.0 air changes per hour the loss will be 95 per cent at the end of the first hour. Fortunately, if there were concomitant, constant production of bacterial contamination of the air, there would be an equal dilution of the bacterial population at the ventilation rates cited.

Conditions of ventilation which lead to the existence of stagnant pockets of air and drafts with marked irregularities of mixing can lead to obvious difficulties in maintaining bactericidal concentrations. These faults can be corrected by the proper use of fans and blower systems to insure that the air in all parts of the treated environment will contain a uniform concentration of glycol vapor.

FACTORS OF IMPORTANCE IN THE DESIGN OF VAPORIZING UNITS

The slow rate of evaporation of triethylene glycol gives rise to difficulties in the production of adequate quantities of vapor. Various techniques have been devised to increase the rate of conversion of liquid glycol into vapor, and, at the present time, heat is commonly used for this purpose. However, there are certain precautions which must be observed in the use of heat for glycol vaporization. Although the boiling point of pure triethylene glycol is approximately 550° F., decomposition of the material becomes significant at temperatures well below this value as indicated by the development of an acrid odor or discoloration of the liquid glycol. Initially it was felt that 260° F. should represent the maximum temperature used for glycol vaporization.[21] However, under experimental conditions, we have observed no apparent decomposition of triethylene glycol when temperatures up to 290° F. were maintained at the site of vaporization, provided the vaporizing unit was designed so that heat was applied to the liquid glycol only at the point of vapor formation. On the other hand, decomposition was frequently observed when the vaporizing temperature was raised above 290° F. or when liquid glycol was kept above 120° F. for long periods of time.

The precise nature of the decomposition products is as yet unknown but they may well be irritant or toxic and their formation should be avoided. For this reason it is felt that a limit of 290° F. should be applied to the temperature employed in vaporization and, furthermore, that liquid glycol should not be heated above 120° F. for long periods of time.

Continuous vaporization is required to maintain adequate concentrations of glycol vapor in the treated environment. The loss of vapor due to condensation on surfaces and air-borne particles and dilution, as a result of ventilation, are so great that intermittent methods of vaporization are inefficient and unreliable. The continuous operation of the vaporizer requires the addition of a suitable glycol reservoir to the unit, otherwise frequent refilling becomes necessary. To prevent decomposition of glycol in the reservoir, its temperature should be kept below 120° F. If this limit is observed, the glycol in the reservoir will show little change over long periods of time.

Because of the low vapor pressure of triethylene glycol there is a marked tendency for the vapor to condense upon cool surfaces and particulate matter in the air. This leads to an appreciable loss of vapor from the air and requires the vaporization of quantities several times greater than those theoretically calculated to produce a desired concentration in a given volume of air. In environments with large areas of cool surfaces, such as windows, the loss of glycol from the air will be correspondingly greater.

In an effort to demonstrate the extent of this loss a series of experiments was performed in a chamber of 640 cu. ft. volume.[22]* Triethylene glycol was vaporized at uniform rates from a constant delivery syringe under varying conditions of ventilation. The temperature employed for vaporization was 285° F. The air was analyzed for glycol content at frequent intervals and the results obtained were compared with the concentrations theoretically calculated to be present under the existing conditions of ventilation. The theoretical concentrations were calculated on the assumption that complete mixing of vapor and air occurred and that the only losses were those due to air exchange.

Rates of vaporization ranging from 0.14 to 1.1 gm. of glycol per hour and ventilation rates ranging from 0 to 2 air changes per hour were studied. In all instances the analytical concentration of glycol vapor was less than 30 per cent of the theoretical value. The results of a typical experiment are shown in Figure 1 in which glycol was vaporized at the rate of 0.58 gm. per hour in the 640 cu. ft. chamber with a ventilation rate of 2.0 air changes per hour and a humidity of 20 per cent. It will be noted that this rate of output was barely sufficient to maintain bactericidal concentrations of glycol vapor in the air under the conditions of the experiment.

It is essential that the rate of glycol vaporization should be sufficient to maintain bactericidal concentrations in the treated environment at all times. The output required for this purpose will vary in different environments, as well as under varying conditions of temperature and humidity. For these reasons a given vaporizer should be capable of various outputs as measured by the grams of liquid glycol vaporized per hour. For small vaporizing units, the output should vary from a minimum of 0.5 gm. to at least 2.0 gm. per hour of liquid glycol vaporized per 1,000 cu. ft. of volume to be treated. These high rates of output are desirable for the purpose of securing bactericidal concentrations in less than one hour after the unit is put into operation and also to compensate for the rapid loss of glycol vapor from the air. Furthermore, a single small vaporizer should not be used for more than one room or for a volume greater than 4,000 cu. ft.

It becomes apparent that the design of a vaporizing unit is of considerable importance in the production of adequate quantities of glycol vapor. The temperatures employed for vaporization, as well as those attained by the liquid glycol in the reservoir, should be carefully controlled. Furthermore, care should be taken to eliminate all fire hazards in the electrical circuits and the unit should be capable of continuous operation over long periods of time. The ultimate requirement, however, is that a given vaporizing unit should maintain bactericidal concentrations of glycol vapor in the air of the space for which it is designed.

When glycol vaporization is to be applied to large areas, such as entire wards or laboratories, the most practical solution is to incorporate a large vaporizing unit or units into the air conditioning system. Care should be taken to provide adequate mixing of the treated air and direct measurements of the glycol content of the air should be made periodically to insure the maintenance of bactericidal concentrations.

Under conditions where chemical analyses are impractical, the presence of a slight fog is essential. The presence of such a fog is not harmful and usually will not be detected unless the observer uses a collimated beam from a brilliant light source. A slight fog would represent the only certain evidence for the presence of bactericidal concentrations of glycol

* The detailed presentation of the data obtained in these experiments will be the subject of a report to be made at a later date.

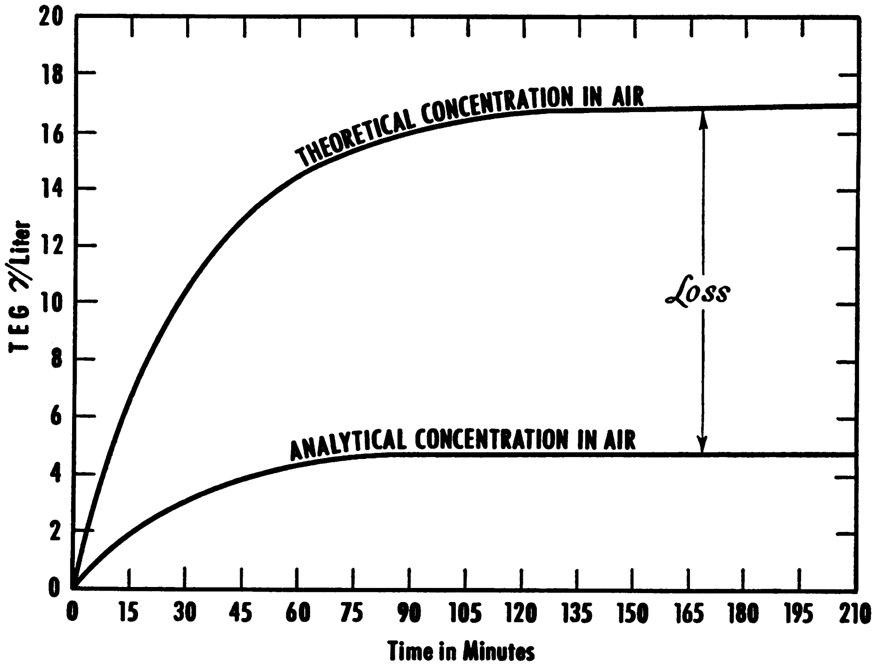

FIGURE 1—Relationship between theoretical (calculated) and analytical concentrations of triethylene glycol obtained in the experimental chamber. Conditions of the experiment were as follows: volume = 640 cu. ft.; two air changes per hour; relative humidity = 20 per cent; rate of glycol vaporization = 0.58 gm. per hour.
Saturation of the air under these conditions equals 5.1 μg./liter.

vapor. The absence of a fog under such circumstances would suggest the possibility of inadequate vapor concentrations and be an indication for increasing the vaporization of triethylene glycol.

ADJUNCTIVE MEASURES

Field studies [23-30] have indicated that complete sterility of the air is not attainable with the use of glycol vapor. However, in every instance in which comparisons were made, it was observed that the aerial contamination was less in the glycol treated than in the control areas. It is believed that the majority of the air-borne organisms which appear to resist the bactericidal action of glycol vapor are dispersed as dried particles from dust reservoirs. This observation leads to the conclusion that oiling of the bedclothes and floor should be used as an adjunct to glycol vaporization. When this is properly done, as was shown by Puck and associates,[24] the aerial contamination approaches a minimum.

The epidemiologic studies on the efficacy of triethylene glycol vapor in the prevention of respiratory disease indicate that the greatest protection occurred in environments with the least opportunity for contact infection.[23-26] The studies which were made in environments in which there was greater opportunity for contact to occur show much less striking protection against infection on the part of glycol vapor.[27-30] This result is to be anticipated and suggests the continued necessity for adequate standards of personal hygiene in the presence of bactericidal concentrations of glycol vapor.

The use of triethylene glycol vapor for aerial disinfection presents few problems from a technical point of view. When the physical requirements for the maintenance of bactericidal concentrations of the vapor are fulfilled, and the proper adjunctive measures applied, significant diminution in the air-borne bacterial contamination of the treated environment can be anticipated. This observation is of significance in situations where the opportunities for air-borne transmission of infection are great, such as in hospitals; particularly in communicable disease wards, nurseries, pediatric units, operating rooms and crowded dispensaries. Other environments, for example, schools, offices, and crowded dwellings, offer interesting possibilities but, until more controlled observations are available, little can be predicted as to the benefit which can be derived from the use of glycol vapor in such locations. In many environments infections are spread by routes other than the inhalation of air-borne microörganisms. Under these circumstances, the benefits to be derived from the use of glycol vapors may well prove to be negligible.

SUMMARY

1. The significance of such factors as relative humidity, temperature, and ventilation in the use of triethylene glycol vapor for aerial disinfection is discussed and the necessity for maintenance of germicidal concentrations in the air of the treated environment is emphasized.
2. Certain features of design applicable to suitable vaporizing units are described and the avoidance of conditions leading to decomposition of liquid triethylene glycol is stressed.
3. The use of oiling of floors and bedclothes and the maintenance of high standards of personal hygiene are indicated as desirable adjuncts to the use of triethylene glycol vapor for aerial disinfection.

REFERENCES

1. Robertson, O. H., Puck, T. T., Lemon, H. M., and Loosli, C. G. The Lethal Effect of Triethylene Glycol on Air-Borne Bacteria and Influenza Virus. *Science* 97:142–144, 1943.
2. Robertson, O. H., Bigg, E., Miller, B. F., Baker, Z., and Puck, T. T. Sterilization of the Air by Certain Glycols Employed as Aerosols. *Science* 93:213–214, 1941.
3. Robertson, O. H., Bigg, E., Miller, B. F., Baker, Z., and Puck, T. T. Sterilization of Air by Certain Glycols Employed as Aerosols and Vapors. *Tr. Assoc. Am. Phys.* 56:353, 1941.
4. Robertson, O. H., Loosli, C. G., Puck, T. T., Bigg, E., and Miller, B. F. The Protection of Mice Against Infection with Air-Borne Influenza Virus by Means of Propylene Glycol Vapor. *Science* 94: 612–613, 1941.
5. Robertson, O. H., Bigg, E., Puck, T. T., Miller, B. F., and Baker, Z. Sterilization of Air by Means of Germicidal Aerosol Mists and Vapors. *A.A.A.S.* No. 17, 1942, pp. 277–280.
6. Robertson, O. H., Bigg, E., Puck, T. T., and Miller, B. F. The Bactericidal Action of Propylene Glycol Vapor on Microörganisms Suspended in the Air. I. *J. Exper. Med.* 75:593–610, 1942.
7. Puck, T. T., Robertson, O. H., and Lemon, H. M. Bactericidal Action of Propylene Glycol on Microorganisms Suspended in the Air. II. *J. Exper. Med.* 78:387–406, 1943.
8. Robertson, O. H., Appel, E., Puck, T. T., Lemon, H. M., and Ritter, M. H. A Study of the Bactericidal Activity *in vitro* of Certain Glycols and Closely Related Compounds. *J. Infect. Dis.* 83: 124–137, 1948.
9. Robertson, O. H. Sterilization of Air with Glycol Vapors. *Harvey Lecture Series* 38:227–234, 1942–1943.
10. Rosebury, T., Meiklejohn, G., Kingsland, L. C., and Boldt, M. H. Disinfection of Clouds of Meningopneumonitis and Psittacosis Viruses with Triethylene Glycol Vapor. *J. Exper. Med.* 85:65–76, 1947.
11. Rosebury, T. *Experimental Air-Borne Infection.* Baltimore: Williams & Wilkins, 1947, p. 47.
12. Bigg, E., and Mellody, M. Fungicidal Action of Triethylene Glycol. *J. Infect. Dis.* 79:45–56, 1946.
13. Robertson, O. H., Loosli, C. G., Puck, T. T., Lemon, H. M., Wise, H., and Lester, W., Jr. Tests for the Chronic Toxicity of Propylene Glycol and Triethylene Glycol on Monkeys and Rats by Vapor Inhalation and Oral Administration. *J. Pharmacol. & Exper. Therap.* 91:52–76, 1947.
14. Puck, T. T. The Mechanism of Aerial Disinfection by Glycols and other Chemical Agents. I and II. *J. Exper. Med.* 85:729–757, 1947.
15. Wise, H., Puck, T. T., and Stral, H. M. A Rapid Colorimetric Method for the Determination of Glycols in Air. *J. Biol. Chem.* 150:61–67, 1943.
16. Kaye, S. Determination of Small Quantities of Triethylene Glycol in Air. *Analytical Chemistry*—In Press.
17. Puck, T. T., Wise H., and Robertson, O. H. A Device for Automatically Controlling the Concentration of Glycol Vapors in the Air. *J. Exper. Med.* 80:377–381, 1944.
18. Puck, T. T., and Wise, H. The Saturation Concentrations of Triethylene Glycol Vapor at Various Relative Humidities and Temperatures. *Science* 105:556–557, 1947.
19. Lester, W., Robertson, O. H., Puck, T. T., Wise, H., and Smith, M. The Rate of Bactericidal Action of Triethylene Glycol Vapor on Microorganisms Dispersed into the Air in Small Droplets. *Am. J. Hyg.* In Press.
20. Unpublished experiments.
21. Robertson, O. H. New Methods for the Control of Air-Borne Infection with Especial Reference to the Use of Triethylene Glycol Vapor. *Wisconsin M. J.* 46:311–317, 1947.
22. Robertson, O. H., Puck, T. T., and Wise, H. The

Construction and Operation of Experimental Rooms for the Study of Air-Borne Infection. *J. Exper. Med.* 84:559–567, 1946.
23. Hamburger, M., Puck, T. T., and Robertson, O. H. The Effect of Triethylene Glycol Vapor on Air-Borne Beta Hemolytic Streptococci in Hospital Wards. I. *J. Infect. Dis.* 76:208–215, 1945.
24. Puck, T. T., Hamburger, M., Robertson, O. H., and Hurst, V. The Effect of Triethylene Glycol Vapor on Air-Borne Beta Hemolytic Streptococci in Hospital Wards. II. The combined action of glycol vapor and dust control measures. *J. Infect. Dis.* 76:216–225, 1945.
25. Hamburger, M., Hurst, V., Robertson, O. H., and Puck, T. T. The Effect of Triethylene Glycol Vapor on Air-Borne Beta Hemolytic Streptococci in Hospital Wards. III. The action of glycol vapors at low relative humidities. *J. Infect. Dis.* 77:177–180, 1945.
26. Harris, T. N., and Stokes, J., Jr. Summary of a Three Year Study of the Clinical Application of Disinfection of the Air by Glycol Vapors. *Am. J. M. Sc.* 209:152–156, 1945.
27. Bigg, E., Olson, F. C. W., and Jennings, B. H. Observations on the Use of Triethylene Glycol Vapors in Military Barracks. *Proc. Central Soc. Clin. Research* 17:38, 1944.
28. Bigg, E., Jennings, B. H., and Olson, F. C. W. Epidemiologic Observations on the Use of Glycol Vapors for Air Sterilization. *A.J.P.H.* 35:788–798, 1945.
29. Bigg, E., Olson, F. C. W., Garlock, F. C., and Jennings, B. H. The Control of Air-Borne Infections by the Use of Triethylene Glycol. *Proc. Central Soc. Clin. Research* 19:67, 1946.
30. Loosli, C. G., Smith, M. H. D., Gauld, R. L., Robertson, O. H., and Puck, T. T. Control of Cross Infections in Infants Wards by the Use of Triethylene Glycol Vapor. *A.J.P.H.* 37:1385–1398, 1947.

Beirut University to Expand

The American University in Beirut, Lebanon, is the largest American educational institution outside the United States. Plans have recently been made for establishing an engineering school, a school of public health, and an agricultural school. Funds have been pledged for the engineering school, which it is expected will eventually graduate 50 engineers annually. Three new courses in agricultural and irrigation engineering, electrical engineering, and petroleum engineering will train men to participate in the development of the area's natural resources.

On the basis of a report by Henry E. Meleney, who spent a semester at the university in 1949 surveying public health educational problems in the Middle East, the Rockefeller Foundation has made a grant of $50,000 as a nucleus for a school of public health administration. For the present a laboratory will be established, courses in public health given, and expenses for survey trips in the area will be made available. At the present time each medical school student must take at least one course in public health problems.

The aim of the university's new program is to develop the resources of the Middle East and combat the poverty and disease that make it one of the world danger spots. President of American University is Stephen B. L. Penrose, Ph.D.